

## Optometric Potpourri

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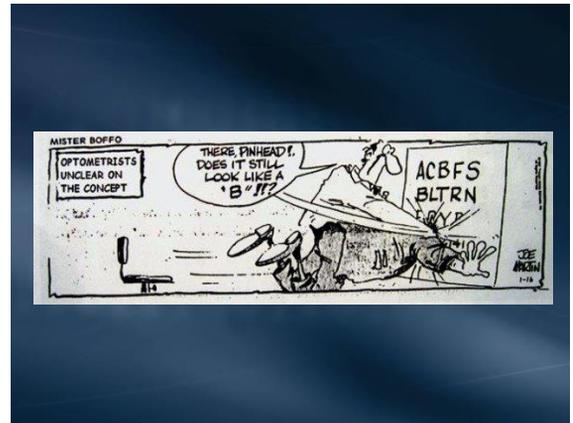


## Disclosures

- Allergan Pharmaceuticals Speaker's Bureau
- Bio-Tissue
- BioDLogics, LLC
- Katena/IOP
- Seed Biotech
- Johnson and Johnson Vision Care, Inc.

## Definition

- Potpourri
  - A miscellaneous collection, a mixture of things



## Urgency vs. Emergency?

## Ocular Emergency

- Immediate threats to the visual system that can lead to permanent loss of visual function if left untreated

## Levels of Urgency

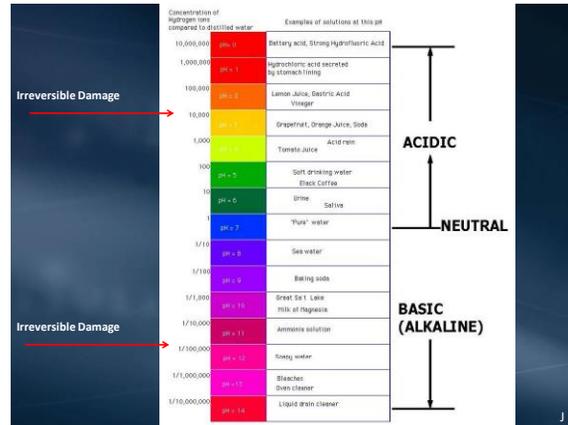
- Immediate: within one to two hours
- Urgent: within 24 hours
- Semi-urgent: within a week
- Routine: within three to six months

## Ocular Emergency?

- Chemical Burn? ✓
- Loss of vision? ✓
- Flashes/Floaters? ✓
- Itching? ✗
- Redness? ✗
- Tearing? ✗
- Discharge? ✗

## Chemical Burn

- Level of Urgency
  - URGENT!!
  - True Ocular Emergency



## Chemical Injuries of the Cornea

- Acid- low pH
- Alkali- high pH
- Irritant- neutral pH
- Surfactants – detergents – neither acid or alkali
  - Cationic, anionic, nonionic
  - BAK
  - Liquid dishwashing detergent
- Modifying factors
  - Duration of contact
  - Solution pH
  - Solution quantity
  - Solution penetrability

## Acid Burns

- Intact corneal epithelium affords moderate protection against penetration of dilute or weak acids
  - Little damage seen unless pH  $\leq$  2.5
  - Acids bind to corneal proteins and act as chemical barrier
  - Severe damage if epithelium removed
- Cause protein coagulation in corneal epithelium
  - Also acts as barrier
  - Ground glass appearance
- Usually non-progressive and superficial
  - Hydrofluoric acid is exception
    - Fluoride ion penetrates stroma
    - Acts as alkali
- Low pH
  - sulfuric acid
  - sulfurous acid
  - hydrochloric acid
  - nitric acid
  - acetic acid
  - chromic acid
  - hydrofluoric acid
- Rates of penetration
  - Sulfuric Acid - slowest
  - Hydrochloric acid - fast
  - Sulfurous acid – faster
  - Hydrofluoric acid -fastest

## Alkali Burns

- Substances that have basic (high) pH
- More severe than acid burns
  - As pH rises, emulsification of lipids in cell membranes occur
    - Destroying barriers to penetration facilitating deeper penetration to anterior segment
  - Injurious effect on stroma involves:
    - Rapid destruction of corneal mucoproteins
      - Resultant stromal haze
      - Increasing as the pH is raised above 11.5
  - Penetrate more rapidly than acids
    - Detectable levels in anterior chamber in seconds to minutes

## Alkali Burns

- 3 most common
  - **\*\*Calcium Hydroxide  $Ca(OH)_2$  (Lime)**
    - Found in plaster
  - **\*Sodium hydroxide NaOH (Lye)**
    - Found in drain cleaners
  - **\*Ammonium hydroxide  $NH_3$  (ammonia)**
    - Found in household cleaners
  - **Potassium hydroxide KOH (Caustic Potash)**
  - **Magnesium hydroxide  $Mg(OH)_2$** 
    - Fireworks - Combined chemical and thermal injury
- **\*\* most common**
- **\* most serious-** penetrates immediately into anterior segment structures



## Treatment - Irrigation

- Irrigation
  - Tetracaine
  - Lid speculum
  - Physiological saline
  - Tap water
- Instruct patient to irrigate with any type of water they have access to
  - Eye wash
  - Sink
  - Garden hose
  - Shower



## Treatment - Irrigation

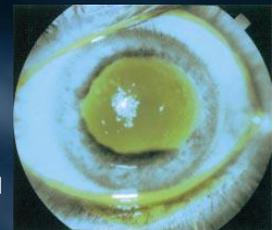
- Must neutralize pH first
  - Goal 7.0 to 7.2
  - Check every 15-30 minutes
    - pH testing OU, even if claims only one eye affected
    - Trapped particles will cause pH change after initial normalization
    - Special attention to fornix



Carolina Biological supplies. [www.Carolina.com](http://www.Carolina.com)

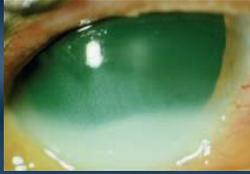
## Grade I

- Involves corneal epithelium only
- Cornea remains clear
  - Epithelium denuded
- Prognosis: Excellent for full recovery of normal corneal appearance and function



## Grade II

- Cornea is hazy, but anterior segment structures are visible
- Prognosis: Good
  - Concerns:
    - Persistent epithelial dysfunction
    - Conjunctivalization
    - Haze
    - Neovascularization



## Grade III

- Stromal haze limits visualization of iris and lens
- Prognosis: Guarded
  - Surgery needed for visual rehabilitation



## Grade IV

- Complete loss of corneal epithelium
- Loss of proximal conjunctival epithelium
- Opaque cornea
  - No view of iris or pupil
- Ischemic necrosis of proximal conjunctiva and sclera
- Prognosis: Extremely poor
  - High risk for sterile ulceration and corneal melt



## Tools of the Trade

## Favorite Instrument

## What Can We Identify?

- Macular Holes
- Macular Degeneration
- Cystoid Macular Edema
- Diabetic Macular Edema
- Central Serous Retinopathy
- Retinal Nerve Fiber Layer (Glaucoma)
- Anterior Segment?

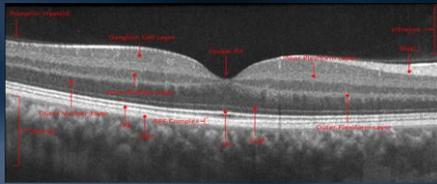
## Optical Coherence Tomography

- Essential tool for non-invasive analysis of retinal tissue for diagnosis and management of retinal disease and glaucoma
- First reported in 1991 by Huang et al
- Provides micron-scale cross sectional images of retina and choroid
- Analogous to B-scan ultrasonography but uses light waves instead of sound waves
  - near infrared light waves (800nm) prevents the need for contact with the globe
- Resolution far exceeds that which can be achieved with ultrasound, computed tomography, or MRI
- Great for patient education
- Allows for quantification and comparison to norms
- Can monitor progression or resolution of disease

## Optical Coherence Tomography

- Time domain 1996-2002
  - Compares a reflected beam of light to a beam of light from a reference center
  - 400 A-scans / sec & 1 B-scan /1.6 sec
  - Resolution 10um
- Spectral Domain
  - Measures difference in wavelength between light from fixed reference that returns to tissue
  - 27,000 A-scans/sec and 512 B-scans
  - Resolution 5um
- Spectral Domain provides more detailed images and more data with improved speed and accuracy

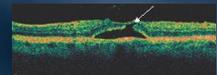
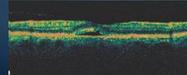
## Normal



- First interface encountered is between the transparent vitreous and reflective NFL
- Deepest layer identified is RPE and choriocapillaris
- Between the two is neuro-sensory retina

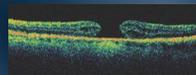
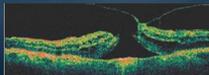
## Macular Holes

- Stage 1
  - Consists of a foveal detachment either with or without a full thickness defect
  - Patients report sudden onset metamorphopsia
- Stage 2
  - Associated with a full thickness defect that can be small or large and can appear slightly eccentric

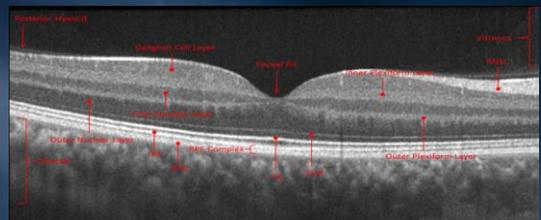


## Macular Holes

- Stage 3
  - Demonstrate larger, complete foveal defect greater than 400um in diameter
- Stage 4
  - Full thickness hole with complete PVD

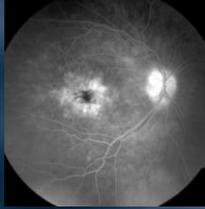


## Normal



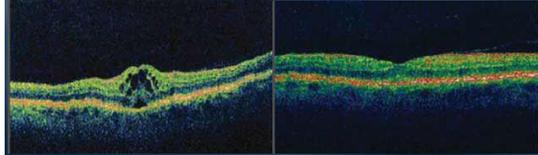
## Cystoid Macular Edema

- Cystoid Macular Edema
  - Causes
    - Medication side effects
    - Trauma/injury
    - Diabetes
    - AMD
    - Cataract surgery



## Delayed Visual Recovery

- Cystoid Macular Edema
  - Most common cause of decreased vision after cataract surgery
  - Usually 4-12 weeks after cataract surgery
  - Incidence?
  - Higher risk patients?

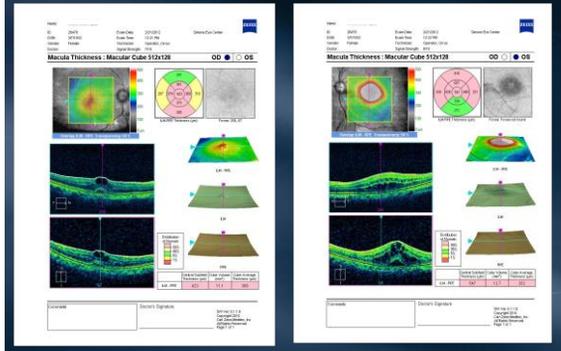


Courtesy of Steven Silverstein, MD

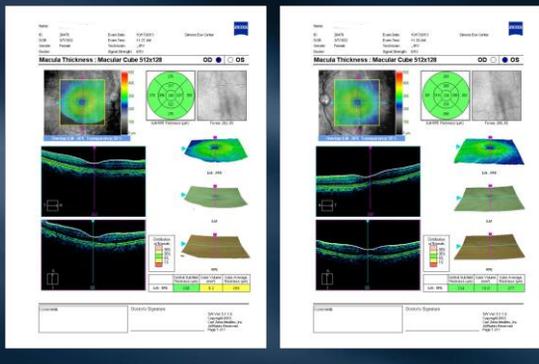
## Case Study

- 81 year old AA female
- Medical history: HTN
- Ocular history: unremarkable
- Uncomplicated cataract surgery
- Uncorrected VA @ 3 months: 20/20 OD, OS
- Returned two months later
  - BCVA 20/30 OD, 20/60 OS

## Case Study

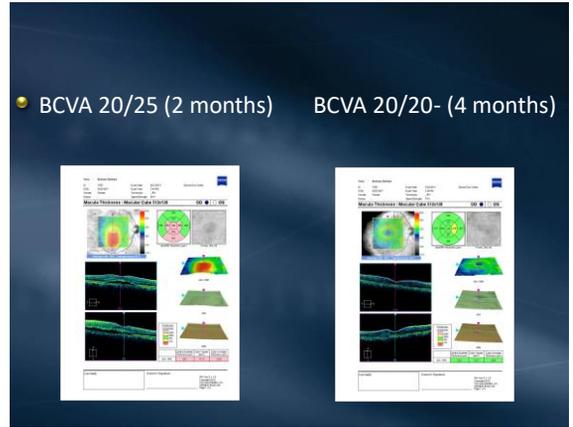
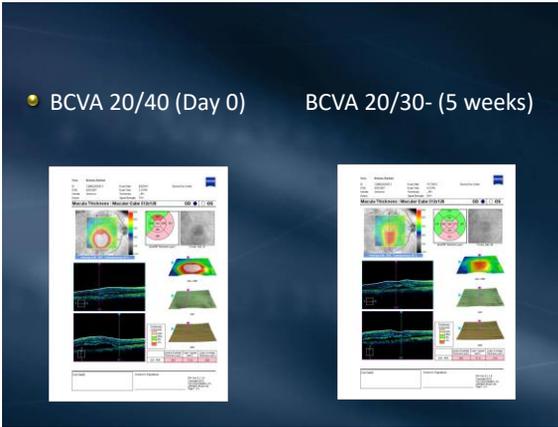


## Case Study



## Case History

- 57 year old white female c/o decreased vision OD for a few weeks
- Medical Hx: Thyroid disease (Synthroid)
- Ocular Hx: DES/Lid Margin disease (Restasis)
- BCVA: 20/40 OD, 20/20 OS
- Differentials?
- What questions do we need to ask?



### Central Serous Retinopathy

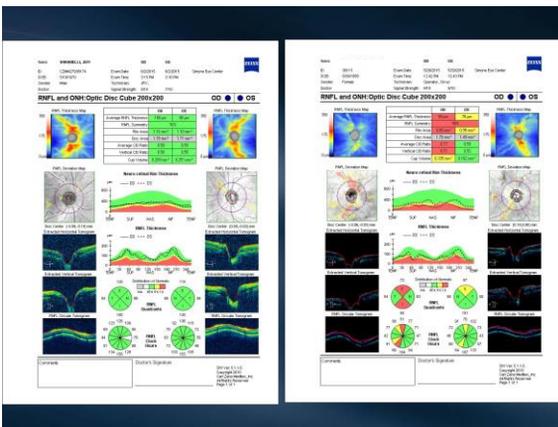
- Localized detachment of sensory retina from underlying pigment epithelium

The figure shows two OCT scans. The left scan shows a normal cross-section of the retina. The right scan shows a localized detachment of the neurosensory retina from the underlying retinal pigment epithelium (RPE), creating a subretinal space filled with serous fluid. Labels on the right scan include: ILM (Internal Limiting Membrane), IPL (Inner Plexiform Layer), ONL (Outer Nuclear Layer), IM (Intermediate Membrane), GCL (Ganglion Cell Layer), NFL (Nerve Fiber Layer), and RPE (Retinal Pigment Epithelium).

### Retinal Nerve Fiber Layer (Glaucoma)

- collects impulses that start with the rods and cones
- carries neural impulses to the optic disc
- lack of function causes loss of visual acuity or scotoma
- lack of function causes the loss of vision in glaucoma patients

The diagram illustrates the Retinal Nerve Fiber Layer (RNFL) as a network of nerve fibers. It shows the fibers originating from the optic disc and extending towards the macula. Labels include: Nasal, Temporal, Optic disc, and Macula lutea.



### Anterior Segment Capabilities

- Can measure corneal thickness
- Can evaluate depth of FB

The figure illustrates three anterior segment capabilities. The top image shows a cross-section of the cornea with labels for 'Epithelial Thickness', 'Stroma', and 'Endothelium'. The middle image shows a blue-lit view of the anterior chamber, likely used for evaluating the depth of a foreign body (FB). The bottom image shows a cross-section of the anterior chamber, possibly used for measuring corneal thickness.

## OCT

- Allows us to manage diseases
  - Monitor progression
  - Monitor improvement

## “These Are a Few of My Favorite Things”



## Disposable Spray Caps

- Convert standard ophthalmic drop bottle to spray bottle
- 12/pack
- \$19.95
- Sigma Pharmaceuticals



## New Therapies in Ocular Surface Disease

## Case Studies

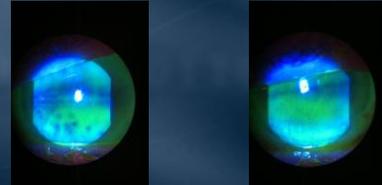
## KeratoConjunctivitis Sicca

## Keratoconjunctivitis Sicca

- Sandra, 75 years old
- Medical Hx:
  - HTN, Osteoporosis
- Ocular History
  - Successful cataract surgery 2012 OU
  - Longstanding dry eye syndrome
- Medications
  - Lotrel
  - Fosamax
  - Restasis
  - FreshKote as needed

## Keratoconjunctivitis Sicca

- Ophthalmic Exam
  - Decreased TBUT
  - Dense and diffuse SPK
  - Patient very photophobic



## Keratoconjunctivitis Sicca

- Options?

## Agenda

- Sutureless Amniotic Membranes
  - Anatomy
  - Options
  - Case Studies
- Autologous Serum Eye Drops
  - Benefits
  - Clinical Indications

## Keratoconjunctivitis Sicca

- Options?



## What is the amniotic membrane

- Innermost layer of the placent
- Thin but tough transparent pair of membranes, which hold a developing embryo (and later fetus) until shortly before birth.
- The primary function of the amniotic membrane is to protect the fe
  1. Anti-inflammatory
  2. Anti-scarring
  3. Anti-angiogenic



## What is the Amniotic membrane

- Amnion is avascular and a translucent membrane composed of an inner layer of epithelial cells which are planted on a basement membrane
- Basement membrane is comprised of Collagen I, III, IV, V and VII, laminin and fibronectin
  - Found in conjunctiva and cornea

## Mechanisms of Action

- Promotes Epithelialization
- Suppresses Inflammation
- Inhibits Scarring
- Inhibits Angiogenesis
- Neurotrophic Factors
- Anti-Microbial Agent

All without the harmful side effects found in topical and oral medications

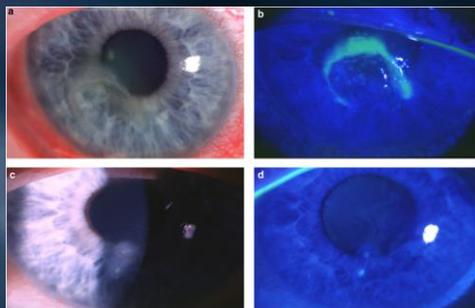
## Indications

- Acute Chemical/Thermal Burns
- Recurrent Corneal Erosions
- Neurotrophic Defects / Persistent Corneal Epithelial Defects
- Filamentary Keratitis
- Vernal Keratoconjunctivitis
- Recalcitrant Dry Eye
- Microbial Keratitis
- Nodular Degeneration
- PRK

## Recurrent Corneal Erosion

- Chronic relapsing disease of corneal epithelium
- Characterized by disturbance of epithelial basement membrane
  - Defective adhesions
  - Recurrent breakdown of corneal epithelium
    - Redness, photophobia, tearing
    - Usually at night or upon awakening
    - May be related to REM during sleep
- Matrix metalloproteinase (MMP)
  - Name for group of enzymes that break down the structure of the extracellular matrix (collagenase)
- Elevated levels of MMP-9 and MMP-2 have been observed in tears of patients with RCE

## Recurrent Corneal Erosions



Courtesy of Ramamurthi et al

## Recurrent Corneal Erosions

### Pathophysiology

- Faulty BM with poor adhesion complexes
  - Poor epithelialization
- Increased MMP

### AM Mech of Action

- Promotes Epithelialization
- Suppresses Inflammation
- Inhibits Scarring
- Inhibits Angiogenesis
- Neurotrophic Factors
- Anti-Microbial Agent

## Recalcitrant Dry Eye

- Clinical findings
  - Tear film instability
  - Ocular inflammation
  - Pro-inflammatory cytokines are upregulated
  - Elevated levels of MMP noted
- Sutureless amniotic membranes contain anti-inflammatory mediators, growth factors and cytokines
  - Help restore a healthy and non-inflamed ocular surface
  - Maintain a stable tear film

## Recalcitrant Dry Eye

### Pathophysiology

- Elevated Pro-inflammatory cytokines
- Elevated levels of MMP

### AM Mech of Action

- Promotes Epithelialization
- Suppresses Inflammation
- Inhibits Scarring
- Inhibits Angiogenesis
- Neurotrophic Factors
- Anti-Microbial Agent

## Procurement

- Membranes are procured and processed according to standards established by American Association of Tissue Banks (AATB) and FDA
- All recovered under full informed consent
  - From Caesarean vs. vaginal
- A thorough medical and social history of donor is obtained. Screened for:
  - Syphilis RPR
  - HIV-1
  - HIV-2
  - HIV type 1 Nucleic Acid Test
  - HTLV-1
  - HTLV -2
  - CMV
  - Hep B Core antibody
  - Hep B surface antigen
  - Hep C Antibody
  - Hep C Virus Nucleic Acid test

## Procurement

- An absolute guarantee of tissue safety is not possible. Allograft has the potential to transmit infections disease to the recipient and the patient should be made aware
- Keep track of tissue used and lot numbers
- All data on file in regard to testing for the tissue
- Do Not use:
  - Areas with active or latent infection
  - Disorder that would create unacceptable risk of post op complications
  - Not to be used in eyes with GLC drainage devices or blebs

## Available Sutureless Membranes



**ProKera®**  
PROKERA PLUS

1-888-296-8858  
7000 SW 97th Avenue  
Suite 211, Miami, FL 33173  
www.biotissue.com  
www.prokerainfo.com



**BioD**

1715 Aaron Brenner Drive Suite  
204 Memphis, TN 38120  
1-877-675-4149  
www.biodlogics.com



**Blythe Medical**

448 Deer Creek Trail  
Hoschton GA 30548 US  
706.654.3209  
http://www.blythemedical.com/  
http://www.seedbiotech.net/



**Ambio-Disk**

3184-B Airway Avenue  
Costa Mesa, CA 1-714-549-1185  
www.iopin.com  
www.katena.com



**katena**



**SKYE BIOLOGICS**

Skye™ OculoMatrix  
2629 Manhattan Beach Blvd.  
Redondo Beach, CA 90278  
Tel. +1 310 796 5680  
orders@skyebiologics.com

## Cryopreserved Amniotic Membranes

## Prokera

Product Specifications	PROKERA   Slim	PROKERA	PROKERA   PLUS
			
Outer Ring Diameter:	21.6 mm	21.6 mm	21.6 mm
Inner Ring Diameter:	17.9 mm	15.5 mm	15.5 mm
Device Height	0.7 mm	1.1 mm	1.1 mm
Tissue Thickness	Single Layer	Single Layer	Multiple Layers
Ring Description	Ring & Elastomeric Band System (polycarbonate)	Dual Ring System (polycarbonate)	Dual Ring System (polycarbonate)

## Prokera

- Cryopreserved
- Store in refrigerator x 3 months 1° C to 10° C (33.8° F to 50° F)
- Store in freezer
  - 1 year between -49° C to 0° C (-56.2° F to 32° F)
  - 2 years between -85° C to -50° C (-121° F to -58° F)
- Shelf life is 2 years from date of manufacturer
- Allow to thaw to room temperature unopened for 5-10 min
- Open inner pouch and remove using blunt forceps
- Rinse with saline to reduce stinging sensation
- Do not leave in eye longer than 30 days

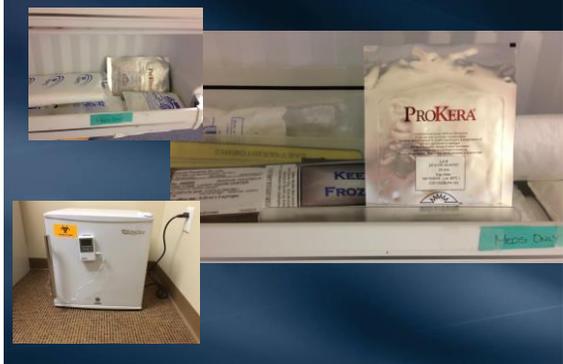
## Prokera



## Prokera



## Prokera





Dehydrated Amniotic Membranes

Alpha Patch (Optix LLC)  
 AmbioDisk (IOP Inc. / Katena)  
 Aril (Seed Biotech)  
 BioDOptix (BioDLogics)  
 Oculomatrix (Skye Biologics)

**Dehydrated Membranes**

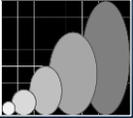
- All stored at room temperature
- Shelf life typically 2-5 years
- Do not need to be rehydrated
- All require the use of BCL

**Dehydrated Membranes**

- Ambio Disk
  - Ambio 2 (35µ)
    - 9 or 15 mm
  - Ambio 5 (100µ)
  - Comes with a Kontur Precision Spherical CL
    - 8.9 bc
    - 16mm\*, 18mm or 20mm
- BioDOptix
  - Two Disc Sizes
    - 12mm or 15mm
  - BCL of choice
    - Careful with sizing
  - 40-60um thick membrane

## Dehydrated Membranes

- Aril
  - 8 mm disc
  - 15 mm disc
  - 2 cm x 3 cm ellipse
  - 3 cm x 5 cm ellipse
  - 3 cm x 7 cm ellipse
- VisiDisc
  - 10 mm disc
  - VisiDisc Thin (45 microns)
  - VisiDisc Thick (200 microns)



## Dehydrated Membranes

- AlphaPatch
  - 1.5cm x 2cm
  - 2cm x 3cm
  - 2cm x 6cm
  - 4cm x 4cm
  - 4cm x 8cm
  - 12 mm disc
- Thought to maintain growth and healing factors
- Not disrupted as may be the case in other dehydrated membranes
- Used currently in wound care
- Extending into ophthalmic setting



- Complete the donor and recipient information form and return immediately

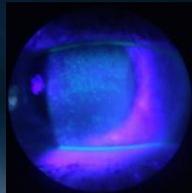


## Case Study- CM

- 62 year old female with DES x 7 years
- Medical history significant for:
  - HTN, hyperlipidemia, anxiety, PTSD, arthritis, osteoporosis, anemia, hypothyroidism, GERD
- Ocular history significant for:
  - Ocular surface disease
- Medications:
  - Synthroid, Elavil, Prilosec, Seroquil, Zocor, Atenolol, Klonopin, Neurontin

## Case Study- CM

- Clinical exam
  - Decreased TBUT OU
  - Lissamine green and NaFl stain
- Unable to continue Restasis
- Decided on amniotic membrane



## Case Study



## Case Study- CM

- Clinical exam
  - Removed ring at 1 week
  - Improved corneal appearance
  - Patient reported improved comfort
- Continue artificial tears
- Long term options reviewed



## Recurrent Corneal Erosion

## Recurrent Corneal Erosion

- WR, 50 year old male
- Initial visit August 2011
- Presented with c/o foreign body/irritation OD
- Medical Hx: HTN, hyperlipidemia
- Ocular Hx: Unremarkable

## Case Study

- Clinical Exam (September 2012)
  - BCVA 20/20 OD, OS
  - Slit lamp exam
    - Blepharitis/Meibomitis
  - DFE
    - Unremarkable
- Clinical Exam (July 2013)
  - Presents with c/o symptoms of RCE OD
    - Cornea clear OD/OS
    - Treatment: Start Muro 128 ointment QHS OD

## Case Study

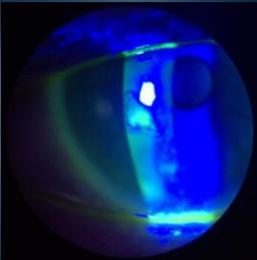
- Clinical Exam (August 2013)
  - Patient more symptomatic
  - Change treatment course

## Case Study

- Clinical Exam (August 2013)
  - Patient more symptomatic
  - Change treatment course
    - Debrided cornea OD
    - BCL x 2 months
    - Add Azasite BID
  - Less symptomatic until January 2014

### Case Study

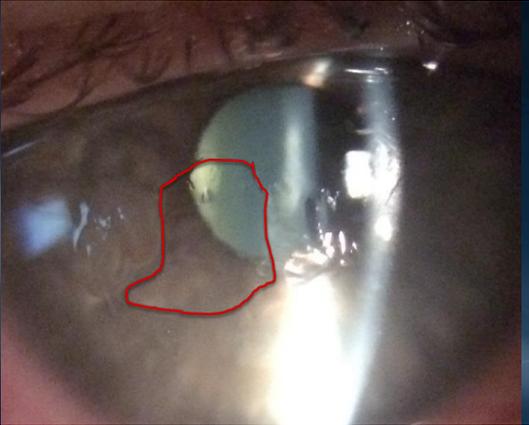
- Clinical Exam (March 2014)
  - New Plan



### Case Study



Debrided cornea



### Case Study




Debrided cornea      ProKera Slim AM inserted

### Case Study

- Clinical Exam (April 2014)



4 days after removal



3 weeks after removal

- Doxycycline 20 mg BID x 2 months
- Lotemax gel TID OD x 1 month

### Autologous Serum

- Use first described in 1984 by Fox et al (for keratoconjunctivitis sicca)

*Fox RI, Chan R, Michelson J, et al. Beneficial effect of artificial tears made with autologous serum in patients with keratoconjunctivitis sicca. Arthritis Rheum. 1984;29:577-83.*

- DEWS / ITF - Severity Level 3 Treatment
- Unpreserved, non-antigenic
- Utilizes patients own blood serum
- Blood is drawn and serum is spun down and mixed with artificial tears / 0.9% sodium chloride
  - Doesn't contain red blood cells and clot factors



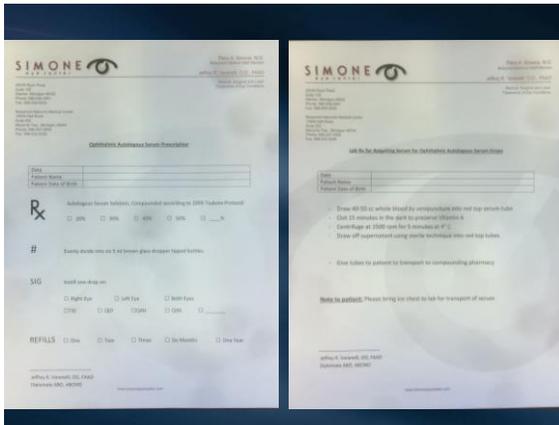


## Autologous Serum

- Contains essential components in tears
  - epidermal growth factor
  - hepatocyte growth factor
  - fibronectin
  - neurotrophic growth factor
  - vitamin A
- Potential complications
  - Immunoglobulin deposits
  - Corneal infiltrates
  - Conjunctivitis
  - Decreased corneal sensitivity

## Autologous Serum

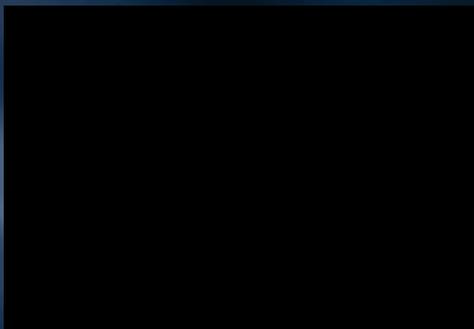
- Concerns:
  - Costly - \$150-300 time, 2-4x /year
    - Typically not covered by insurance
  - Inconvenient - Requires blood donation from patient
  - Need to store frozen for up to three months at -20°C
  - Keep away from light to avoid degradation of Vitamin A
  - Possible risk of infection
    - Cornea and systemic



## Compounding Pharmacy

Physician's Compounding Pharmacy  
 1900 S. Telegraph Road, Suite 102  
 Bloomfield Hills, MI 48302  
 Phone: 248-758-9100  
 Fax: 248-758-1831

## Newer Technologies



## Anterior Segment Therapies

- Product Design
  - Disease-specific, tailored drug release and plug persistence
- Procedure
  - Easy to insert, familiar procedure to physicians
  - Non-invasive
  - Absorbable – no need for removal
  - Allows for visualization by the patient and the physician



Courtesy of Ocular Therapeutics

## Sustained Release Dexamethasone

- Value Proposition - *Strong steroid, soft delivery*
  - \* 1x administration replaces 4x/day dosing over 4-week period
  - \* Plug tailors release with tapered administration for 30 days
  - \* 7% of the drop equivalent dose; no IOP spikes observed in Phase 2
- Plug characteristics
  - \* Easy to insert
  - \* Comfortable for the patient
  - \* Absorbable – no need for removal
- Status
  - \* Phase 3 trials complete for post-op inflammation and pain
  - \* Topline results reported for Phase 2 trial for allergic conjunctivitis



Courtesy of Ocular Therapeutics

## Sustained Release Dexamethasone Plug Insertion and Visualization



Courtesy of Ocular Therapeutics

## New Technologies and Ideas are Great

Most of the time.....



## Thank you



Please feel free to contact us:

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